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The Familial Aggregation of Depressive Symptoms, Antisocial Behavior, and Alcohol Abuse

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This study describes results from an ongoing family study of adolescent boys and their families designed to investigate potential risk factors for substance abuse. The adolescent treatment probands have severe drug and alcohol related problems and were recruited through a residential rehabilitation program. To date, the sample includes 251 individuals: 39 male probands and their families and 34 control families matched for age and geographic location (zip code). Probands and participating family members are given a structured interview which assesses alcohol and drug problems, and various psychiatric symptoms. The purpose of the present study was to examine the coaggregation of depressive symptoms, antisocial behavior, and alcohol misuse. Multivariate pedigree analyses were performed using a model that allowed for the estimation of vertical familial transmission, residual sibling resemblance, and assortative mating. Spouse correlations were estimated at .57, .21, and .31 for antisocial behavior, depressive symptoms, and alcohol abuse, respectively. Residual sibling environment (i.e., sibling resemblance unaccounted for by parent–offspring transmission) was not found for alcohol problem symptoms, but did contribute to resemblance for antisocial behavior and depressive symptoms. The proportion of variance accounted for by vertical familial transmission was estimated at approximately 30 to 40%. More important, correlations among the transmissible family factors for these psychiatric syndromes ranged from .58 to .73, suggesting substantial overlap among the underlying familial antecedents for these disorders. Am. J. Med Genet. 74:183–191, 1997 © 1997 Wiley-Liss, Inc.

KEY WORDS: depression; antisocial behavior; alcohol abuse; family study; comorbidity; adolescence

INTRODUCTION

Developmental studies of adolescent behavior consistently report that alcohol and drug abuse are correlated with more general forms of deviance, particularly conduct disorder symptoms [Jessor and Jessor, 1975; Jessor and Jessor, 1977; Watts and Wright, 1990; Weber et al., 1989; Windle, 1991]. However, there is increasing evidence that depression may be involved in the transition from substance experimentation to substance abuse. A number of researchers have found associations between depression, suicide attempts, and substance abuse [Berman and Schwartz, 1990; Deykin et al., 1987; Henry et al., 1993; Kienhorst et al., 1990; Riggs et al., 1995; Robbins and Alessi, 1985; Stefanis and Kokkevi, 1986; Weiss et al., 1992], and the prevalence of depression in referred groups of juveniles with conduct disorder (CD) is substantially higher than in the population [Zoccolillo, 1992].

While the frequent incidence of comorbidity in clinical populations has been well established, it remains unclear what biological and/or socio-cultural factors may underly the development of these comorbid conditions. There is increasing evidence for the coaggregation of depressive symptoms [Goldstein et al., 1994; Merikangas and Gelernter, 1990; Rounsaville et al., 1991] and antisocial behavior [Cadoret et al., 1986; Cadoret et al., 1987; Grove et al., 1990] in the families of substance abusers. Studies of the psychiatric symptoms co-occurring within and among relatives provide a unique opportunity to estimate the magnitude of genetic and family environmental influences on the development of these syndromes. Although to date the data remain inconclusive, there is accumulating evidence that genetic factors play an important role in the familial aggregation of these psychiatric syndromes.

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The findings are perhaps most consistent for the etiology of alcoholism. The preponderance of data from twin and adoption studies is consistent with a substantial genetic contribution to alcohol-related problems [for reviews see Goodwin, 1979; Goodwin, 1985; Heath et al., 1997; McGue, 1993]. Consistent results for illicit drugs are more limited, but the findings generally support genetic contributions to the abuse of illicit drugs as well [Anthenelli and Schuckit, 1992; Cadoret et al., 1986; Grove et al., 1990]. Genetic factors have also been implicated for the development of depression [Kendler et al., 1993; Kendler et al., 1994; Wierzbicki, 1986] and antisocial behavior [Caspi and Moffitt, 1995; Cloninger and Gottesman, 1987; Dishion et al., 1995; Mednick et al., 1988; Moffitt, 1993; Rutter et al., 1990] in both clinical and epidemiological samples.

The substantial co-morbidity observed for substance abuse, antisocial behavior and depression, and the converging evidence for the importance of genetic influences on these disorders, suggests the need for examining the possibility that common etiological factors may underlie these psychiatric syndromes. The purpose of the present study was to investigate the role of depression and antisocial behavior in problem alcohol use. The primary goals of the study were to: 1) confirm the phenotypic association among antisocial behavior, alcohol use problems, and depressive symptoms, and 2) examine the extent to which familial transmissible factors contribute to these phenotypic relationships. In addition, researchers have suggested that sibling imitation effects may also play an important role in substance abuse [Brook et al., 1986; McGue et al., 1996; Rowe and Gulley, 1992]. Thus, in this study we also examine whether there is evidence for additional familial resemblance among siblings that cannot be explained by transmissible factors from parents to children.

METHOD

Sample

This report utilizes data from the Adolescent Substance Abuse (ASA) study, an ongoing family study at the Institute for Behavioral Genetics at the University of Colorado, Boulder. The treatment probands are male adolescent substance abusers aged 13 to 18 years, referred by social service and juvenile justice agencies for substance use and delinquency to a public, milieu-type residential treatment facility in the Denver Metropolitan area. The probands in this study were drawn from consecutive admissions to the program. However, it should be noted that approximately 30% elope from the open facility prior to assessment and another 15% of the families refuse to participate. Families with at least one consenting biological relative are included. Data are obtained from all relatives and cohabitants of the probands who: 1) consent to the interview, 2) are at least 11 years of age, and 3) have resided with the proband for at least one year. Family history data for all relatives who are not directly interviewed is obtained from all participating family members. Degree of relationship between relatives (e.g., paternity) is based on family report. No independent verifications were conducted.

Control probands are male adolescents matched within one year of age to the treatment probands and also by zip code of residence. Recruitment of these adolescents and their families was carried out by a private research firm by randomly querying public phone lists within specified zip codes. Refusal rates for the controls were not recorded. Thus, this control sample should be considered a volunteer community sample due to informed consent requirements. All subjects were paid $20 for participation.

The numbers of individuals on whom we have obtained data, broken down by relationship to the probands, are presented in Table I. A description of the demographics of the parents of the probands participating in the study appears in Table II. The control sample was meant to provide a representative sample of the population. Although probands were matched by age and zip code of primary residence, control family relatives were not matched to the treatment relatives in any way. Note that the parents of the control probands had more education, higher-level occupations, and greater family income than the parents of the treatment probands. The ethnicity of the treatment and control families also differed somewhat, with control families more representative of the ethnic composition of the state of Colorado. Use of such a control sample assumes that socio-economic status is more a consequence than a causal factor of psychopathology. To the extent that the opposite is true, some caution in the interpretation of our results is warranted. In all likelihood, both processes are operating.

Measures

Family members aged 18 and over were administered the version of the NIMH Diagnostic Interview Schedule (DIS) current in 1989 [Robins et al., 1989]. This interview included sections on major depression and dysthymia, and antisocial personality (ASP). Adult depressive and ASP symptom scores were derived by summing lifetime symptom counts from this interview. Depressive symptoms were scored by summing items from the major depression and dysthymia sections.

TABLE I. Sample Sizes

	ASA Study	
	Treatment	Control
Probands	39	34
Mothers	24	29
Fathers	11	25
Sisters	5	20
Brothers	9	21
Other relatives	12	8
Unrelated[a] cohabitants	11	3
Adult males	25	30
Adult females	35	40
Juvenile males	44	52
Juvenile females	7	18
Total	111	140

[a]Unrelated refers to non-biological relatives/cohabitants.

TABLE II. Parent Demographics (Percent Categories)

	Treatment		Control	
	Mothers	Fathers	Mothers	Fathers
Ethnicity				
White	62	56	81	88
Black	4	6	6	0
Hispanic	21	33	10	8
Other	12	0	3	4
Occupation				
Professional	8	28	48	33
Semi-professional	17	17	6	29
Clerical, skilled, retail	25	28	16	17
Farmer	4	11	0	0
Semi-skilled	4	17	6	17
Unskilled	12	0	3	4
Homemaker	17	0	19	0
Student	4	0	0	0
Education				
Grade school	8	0	3	0
Some high school	33	11	0	4
High school graduate	33	33	26	17
Technical school	0	6	10	8
Some college	12	44	13	25
College graduate	0	0	19	29
Graduate degree	4	6	26	17
Income				
<\$5000	4	0	3	0
\$5000–\$10,000	25	0	0	4
\$10,000–\$15,000	8	33	3	4
\$15,000–\$20,000	17	6	6	0
\$20,000–\$35,000	21	44	23	21
\$35,000–\$50,000	8	11	23	29
>\$50,000	8	6	39	42

Note: Percentages may not sum to 100 due to missing responses.

The probands and all relatives of the probands under the age of 18 were administered the Diagnostic Interview for Children and Adolescents (DICA) [Reich & Welner, 1989]. The DICA included sections on major depression, dysthymia, and conduct disorder (CD). As with the adults, a depressive symptoms score was derived by summing lifetime depression and dysthymia symptoms. A CD score was derived by summing symptom counts weighted by their frequency. This ordinal weighting scheme (3-point scale) is determined by the DICA. For example, items such as frequency of school suspensions were weighted such that four or more times was given a greater score (3) than two to three times (2), or only once (1). We used the CD score in children as a comparable measure to the ASP symptom counts in the adults. This assumes CD and ASP are aspects of a single dimension of antisocial behavior, which has found some support in the literature [Caspi and Moffitt, 1995; Dishion et al., 1995; Loeber, 1991; but see also Gottesman and Goldsmith, 1994; and Lyons et al., 1995]. Hereafter, we refer to these scores (CD and ASP) as indices of antisocial behavior (ASB).

Alcohol problem counts were obtained from the Substance Abuse Module of the Composite International Diagnostic Interview (CIDI-SAM; Robins et al., 1983). Lifetime problem counts were derived by summing across frequency, abuse, and dependence items from the CIDI-SAM, employing identical scoring algorithms for adults and juveniles.

We have chosen to analyze problem counts and frequencies instead of DSM-III-R diagnoses to provide continuous rather than dichotomous scalings of the disorders of interest. The use of continuous measurements provides considerably more power in our statistical analyses, and minimizes misdiagnosis problems in individuals who have not passed through the age of risk. For example, many of our younger juveniles would not meet DSM criteria, but do show measurable symptoms. Biserial correlations between these problem counts and diagnostic categories range between .82 and .94, suggesting that the problem counts are capturing comparable information. Due to marked skewness of the problem counts, analyses were performed on both raw counts and rank normalized [Blom, 1958] scores.

Tau model

Since the present data sets are not optimally genetically informative, familial transmission was explored using a multivariate Tau model [based on Rice et al., 1978]. The correlational parameters in the model are 1) a diagonal matrix, $\mathbf{t}$, of familial transmission parameters, 2) $\mathbf{R}_t$, a symmetric matrix of correlations among the transmissible latent factors, 3) a symmetric covariance matrix, $\mathbf{C}_U$, among the latent residual nontransmissible components, 4) a symmetric covariance matrix, $\mathbf{C}_S$, among the residual factors for siblings reared together (i.e., residual sibling environment and/or nonadditive genetic factors shared by siblings), and 5) $\mathbf{D}$, a matrix of phenotypic marital assortment paths. The model is parameterized in terms of correlations rather than covariances, so standard deviations for adult and juvenile males and females are also estimated and used to obtain the expected covariance matrices. Figure 1 shows a path diagram of the multivariate Tau model for an extended three-generation pedigree which includes multiple spouses and half-siblings. The expected correlation matrices for all the relationships in the present dataset are given in Table III. Due to potential cohort effects, and because different measures were

TABLE III. Expectations

Relationship	Symbol	Expected correlation matrix
Within-person	$\mathbf{R}_P$	$\mathbf{tR}_t\mathbf{t}' + \mathbf{C}_U$
Mates	$\mathbf{R}_M$	$\mathbf{R}_P\mathbf{DR}_P$
Offspring/parent	$\mathbf{R}_{OP}$	$\frac{1}{2}\mathbf{tR}_t\mathbf{t}' + \frac{1}{2}\mathbf{tR}_t\mathbf{t}'\mathbf{DR}_P$
Siblings	$\mathbf{R}_{Sib}$	$\frac{1}{2}\mathbf{tR}_t\mathbf{t}' + \frac{1}{2}\mathbf{tR}_t\mathbf{t}'\mathbf{DtR}_t\mathbf{t}' + \mathbf{C}_S$
Grandoffspring/grandparent	$\mathbf{R}_{GO,GP}$	$\frac{1}{2}\mathbf{R}_{OP} + \frac{1}{2}\mathbf{tR}_t\mathbf{t}'\mathbf{DR}_{OP}$
Niece (nephew)/uncle (aunt)	$\mathbf{R}_{\mathrm{Avun}}$	$\frac{1}{4}\mathbf{tR}_t\mathbf{t}'(\mathbf{I} + \mathbf{DtR}_t\mathbf{t}' + 2\mathbf{DR}_{Sib})$
Half-siblings	$\mathbf{R}_{H\text{-}Sib}$	$\frac{1}{4}\mathbf{tR}_t\mathbf{t}' + \frac{1}{2}\mathbf{tR}_t\mathbf{t}'\mathbf{DtR}_t\mathbf{t}' + \frac{1}{4}\mathbf{tR}_t\mathbf{t}'\mathbf{DR}_P\mathbf{DtR}_t\mathbf{t}'$
Cousins[a]	$\mathbf{R}_{Cuz}$	$\frac{1}{4}\mathbf{t}(\mathbf{X} + \mathbf{Y} + \mathbf{Y}' + \mathbf{Z})\mathbf{t}'$
Serial mates	$\mathbf{R}_{SM}$	$\mathbf{R}_P\mathbf{DR}_P\mathbf{DR}_P$
Step-child/step-parent	$\mathbf{R}_{SC,SP}$	$\mathbf{R}_{OP}\mathbf{DR}_P$
Offspring-in-law/parent-in-law	$\mathbf{R}_{OP\text{-}IL}$	$\mathbf{R}_P\mathbf{DR}_{OP}$
Sibs-in-law	$\mathbf{R}_{Sib\text{-}IL}$	$\mathbf{R}_{Sib}\mathbf{DR}_P$

[a]Let $\mathbf{X} = \frac{1}{2}\mathbf{R}_t + \frac{1}{2}\mathbf{R}_t\mathbf{t}'\mathbf{DtR}_t$, $\mathbf{Y} = \mathbf{R}_t\mathbf{t}'\mathbf{DtX}$, and $\mathbf{Z} = \mathbf{R}_t\mathbf{t}'\mathbf{DtR}_{Sib}\mathbf{DtR}_t$.

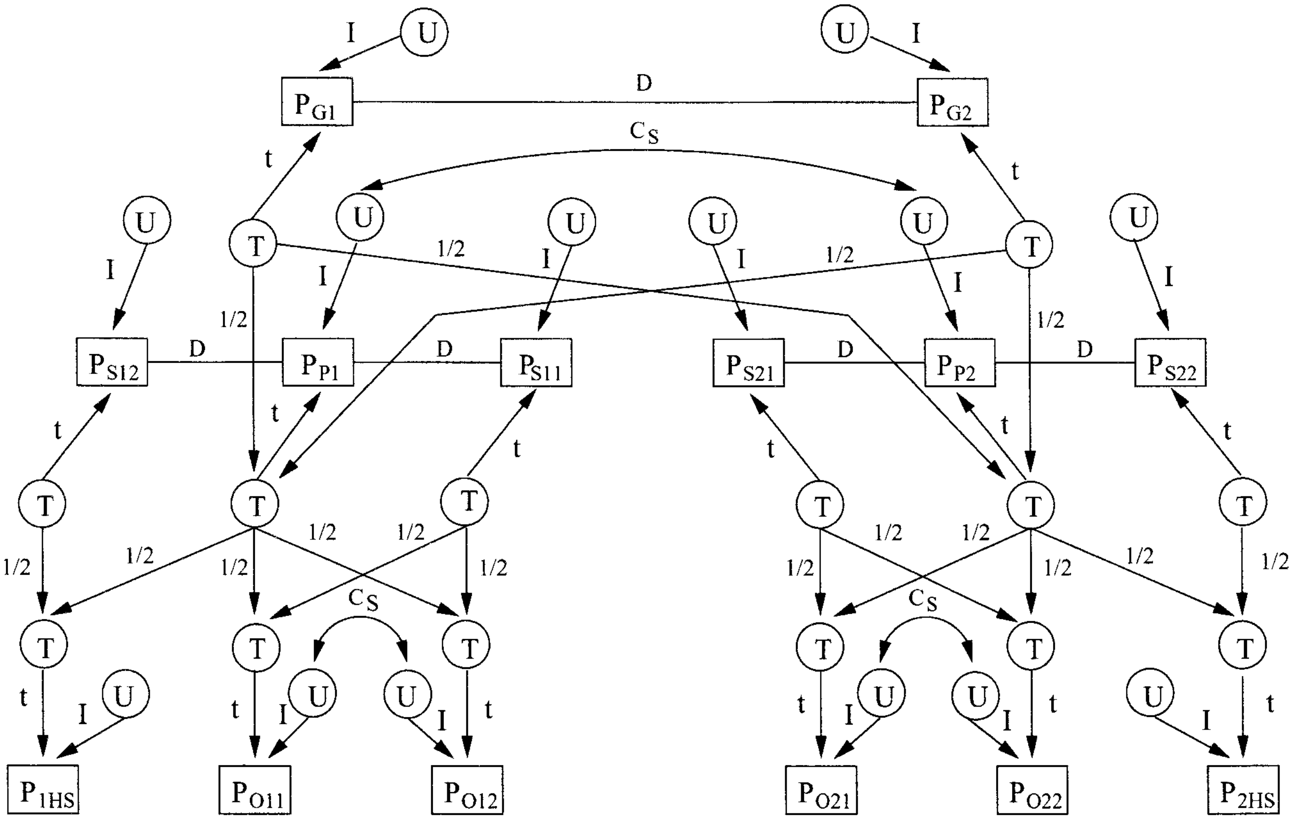

Fig. 1. Multivariate Tau model for a three-generation extended pedigree, including multiple/serial spouses and half-siblings. P = vector of observed phenotypic scores; T = vector of latent transmissable factors; and U = vector of latent nontransmissable factors. The subscripts G, P, O, S and HS refer to grandparents, parents, offspring, spouses, and half-siblings, respectively.

used for adults and adolescents for the depressive and antisocial symptoms, our analyses modeled different means and variances for the adult and adolescent age cohorts, as well as for males and females, for all measures.

Pedigree Analysis

Because the data are from unbalanced pedigrees, modeling was performed using Maximum-Likelihood (ML) estimation of the raw data [Lange et al., 1976]. The negative of the following ML pedigree log-likelihood (LL) function was minimized:

$$LL = \sum_{i=1}^{N} \left[-\frac{1}{2} \ln \, |\mathbf{\Sigma}_i| - \frac{1}{2} (\mathbf{x}_i - \boldsymbol{\mu}_i)' \mathbf{\Sigma}_i^{-1} (\mathbf{x}_i - \boldsymbol{\mu}_i) \right] \tag{1}$$

where,

- $\mathbf{x}_i$ = vector of scores for k measures for pedigree i,
- $\mathbf{\Sigma}_i$ = appropriate expected covariance matrix for pedigree i,
- N = total number of pedigrees,
- $\boldsymbol{\mu}_i$ = vector of expected means for k measures in each family,

and where,

$$2(LL_1 - LL_2) = \chi^2 \tag{2}$$

for testing the difference between two alternative models. Four expected means were estimated for each of the three measures: 1) a mean for adult males, 2) a mean for adult females, 3) a mean for juvenile males, and 4) a mean for juvenile females. For these analyses, we are assuming that there is direct selection on the treatment proband means for each measure, but not on the variances or covariances. That is, the means for a given class of relatives on a vector of measures, **y,** after selection is denoted as $\boldsymbol{\mu}_y^*$ and is given by:

$$\boldsymbol{\mu}_y^* = \boldsymbol{\mu}_y + \mathbf{B}_{yx}(\boldsymbol{\mu}_x^* - \boldsymbol{\mu}_x), \tag{3}$$

where $\boldsymbol{\mu}_y$ is the vector of means in the unselected (control) population, and $\mathbf{B}_{yx}$ is the matrix of unstandardized regression coefficients of the relatives' scores, **y,** on the selection variables, **x,** for the juvenile control probands. The selection function, $(\boldsymbol{\mu}_x^* - \boldsymbol{\mu}_x)$, is simply the mean of the treatment probands on the variables of selection ($\boldsymbol{\mu}_x^*$) minus the unselected means ($\boldsymbol{\mu}_x$), estimated directly from the control sample probands.

The assumption that selection is on the means only (i.e., the covariance structure is unaffected by selection) appears reasonable given the striking similarity between the observed covariance structure within the treatment and control groups. Moreover, the variances appear to be slightly larger in the treatment sample than for the controls, which is contrary to what the effects of truncation selection would predict. Table IV shows the observed covariance structure for the transformed (rank-normalized) variables used in our modeling analyses. The variances and covariances for the

TABLE IV. Observed Covariance Structure for Control and Treatment Families

	ASB	Depression	Alcohol
Controls	.661	.391	.463
		.871	.311
			.761
Treatment	.723		
	.239	1.014	
	.516	.241	.856

control subjects (computed from all family members) are in the upper triangle of the matrix, and the covariance structure for treatment subjects is shown in the lower triangle. A test for the equality of the covariance structure across the two groups confirmed their similarity [$\chi^2_{(6)} = 8.73, p = .189$].

RESULTS

Descriptive Statistics

Means and standard deviations for depressive symptoms, ASB, and alcohol problem symptoms are shown in Table V. Adult (DIS) and juvenile (DICA) symptom counts for depression and ASB are not directly comparable, due to the use of different assessment interviews. Alcohol problems were assessed using the CIDI-SAM for both adults and juveniles.

TABLE V. Means and Standard Deviations for First-Degree Relatives

	Treatment			Control		
	M	SD	N	M	SD	N
	Depressive symptoms					
Juveniles:						
Probands[a]	15.8	9.4	39	9.4	7.8	34
Brothers	10.3	6.8	4	7.1	6.5	18
Sisters	17.0	9.5	4	10.7	9.2	15
Adults:						
Fathers[b]	6.8	5.8	11	2.4	3.2	25
Mothers	7.9	6.7	24	5.2	6.2	29
Brothers	2.2	2.2	5	4.0	1.0	3
Sisters	3.0	0.0	1	7.3	5.2	5
	Antisocial symptoms					
Juveniles:						
Probands[a]	30.6	8.4	39	9.0	6.1	34
Brothers	21.3	14.9	4	6.6	5.8	18
Sisters	9.0	4.5	4	2.9	3.1	15
Adults:						
Fathers[b]	9.2	7.1	11	4.0	3.0	25
Mothers[a]	4.2	3.4	24	1.8	1.8	29
Brothers[b]	12.6	4.8	5	3.7	2.9	3
Sisters	4.0	0.0	1	4.0	4.5	5
	Alcohol problem counts					
Juveniles:						
Probands[a]	25.5	9.5	39	7.6	8.1	34
Brothers	12.0	14.0	4	2.7	5.0	18
Sisters	6.0	3.7	4	1.9	4.2	15
Adults:						
Fathers	10.5	9.1	11	5.2	5.7	25
Mothers[b]	3.7	5.5	24	0.6	1.2	29
Brothers	10.8	5.2	5	3.7	3.2	3
Sisters	0.0	0.0	1	3.0	2.6	5

[a]$p < .01$, [b]$p < .05$ (Between-group t-tests).

Note that fairly large mean differences between treatment and control probands were found for all of the measures. In addition, all adult first-degree relatives (mothers, fathers, and siblings) showed significantly greater numbers of antisocial symptoms than control family first-degree relatives. However, only fathers of the treatment probands showed significantly greater depression, and only mothers showed significant differences for alcohol problem symptoms. Although differences are not statistically significant for some of the measures for some relative types, these differential patterns should be interpreted with some caution, due to the fairly small sample sizes, particularly for fathers and siblings. Note that all of the means for first-degree relatives of treatment families vs. control family relatives were in the expected direction, with treatment family members showing greater numbers of problems for all measures.

Model Fitting

Model fitting analyses were used to investigate the sources of familial aggregation for depression, ASB, and alcohol problems. A series of nested model comparisons were performed both to determine which sources of variation and covariation are needed to explain these data and to arrive at the most parsimonious explanation for the comorbidity of these disorders. Analyses were carried out using raw problem counts and rank-normalized scores. Figure 2 shows within-individual parameter estimates from fitting the full Tau model to rank-normalized scores (A) and raw score counts (B). Since nearly identical results were obtained, all subsequent results are based on rank normalized counts only.

Model comparisons are presented in Table VI. Comparison of Model 1 (the full Tau model described above) with Model 2 provides a test of whether residual sibling environment contributes to the covariation among the different problems. This model comparison suggests that there were no significant residual sibling correlations underlying the comorbidity of ASB, depression, and alcohol problems. However, note that there was evidence for residual sibling effects specific to each of the problems (Model 3 vs. Model 1). That is, although sibling effects did not contribute to comorbidity, there was sibling resemblance specific to depressive symptoms and ASB that could not be explained by vertical familial transmission. This is evident from the parent–offspring and sibling correlations estimated from the full model and shown in Table VII. Note that the sibling correlations are nearly twice the parent–offspring correlations for ASB and depressive symptoms, but are comparable for alcohol abuse.

The residual sibling correlations for ASB and depressive symptoms were estimated at .34 and .39, respectively. Converting these to phenotypically standardized covariances suggests that approximately 50% of the expected sibling correlations for these disorders cannot be explained by factors transmitted from parents to offspring. The residual sibling correlation spe-

TABLE VI. Model Comparisons

Model	Form	$-LL$[a]	NP[b]	χ^2	*df*	*p*
1	Full Tau model	69.37	48			
2	Model 1, drop off-diagonal $\mathbf{C}_S$	71.32	45	3.90	3	.27
3	Model 2, drop $\mathbf{C}_S$	79.08	42	15.52	3	<.01
4	Model 2, drop $\mathbf{D}$	78.22	39	13.80	6	<.05
5	Model 2, drop $\mathbf{R}_{t_{ASB,ALC}}$	78.66	44	14.68	1	<.01
6	Model 2, drop $\mathbf{R}_{t_{ASB,DEP}}$	77.96	44	13.28	1	<.01
7	Model 2, drop $\mathbf{R}_{t_{ALC,DEP}}$	73.09	44	3.54	1	.06
8	Model 2, drop off-diagonal $\mathbf{C}_U$	80.89	42	19.14	3	<.01

[a]log-likelihood function.
[b]number of free parameters.

cific to alcohol problems was estimated at .10, but could be constrained to zero in this data without adversely affecting model fit.

Since Model 3 could be rejected, Model 2 was then used as the base model for subsequent comparisons. A test of assortative mating, or spousal correlations, for the problem symptoms indicated that spousal resemblance was substantial (Model 4). Estimates of the spousal correlations are shown in Table VIII. These correlations suggest that there is strong assortment and/or cohabitation effects for ASB, with more moderate marital assortment for depressive symptoms and alcohol abuse.

Tests for familial transmission, and for the individual correlations among the transmissible factors, are tested by comparing Model 5 through Model 7 with Model 2. Note that there are no distinct tests of the transmission parameters $\mathbf{t}$ independent of the correlations among the transmissible factors $\mathbf{R}_t$. That is, one cannot constrain one of the transmission parameters to zero without also constraining the relevant correlations among the transmissible factors to zero as well.

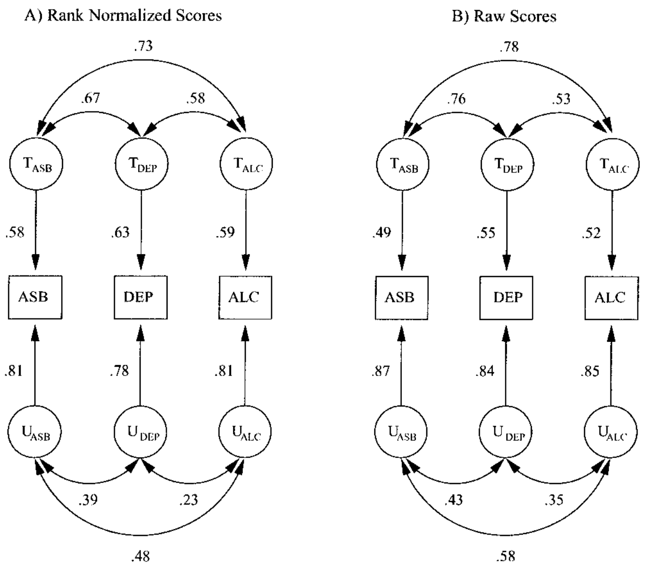

Fig. 2. Estimates for within-individual parameters from fitting a trivariate Tau model to (**A**) rank-normalized symptom counts, and (**B**) raw symptom counts. $\mathbf{T}$ = latent transmissible family factors and $\mathbf{U}$ = latent residual non-transmissible factors. Directed arrows represent path coefficients and bi-directional arrows represent correlations among the latent factors. The U_j are obtained by subtraction ($U_j = \sqrt{1 - t_j^2}$).

Therefore, tests of the individual transmission parameters are unnecessary and redundant with the results shown here.

Estimates of the proportion of variance explained by transmissible family factors were 34%, 40%, and 35% for ASB, depressive symptoms, and alcohol problems, respectively. More important, these model comparisons show that, with the exception of the correlation between depressive symptoms and alcohol problems, the transmissible familial antecedents underlying these measures are substantially intercorrelated. Further, the nonsignificant correlation between depressive symptoms and alcohol problems (Model 7) was not trivial in magnitude (see Fig. 2). Constraining this correlation to zero resulted in a reduced model fit that just missed statistical significance at the nominal .05 level.

Finally, non-transmissible factors specific to individuals accounted for approximately 60–65% of the variation in ASB, depressive symptoms, and alcohol problems (see Fig. 2). Model 8 tests whether such non-transmissible factors also contribute to the covariation among the measures. As expected, the relatively poor fit of Model 8 suggests that factors unique to the individual, such as unique environmental experiences that are not transmitted from parents to children or shared by siblings, also contribute substantially to the observed comorbidity among these different disorders.

DISCUSSION

There is substantial evidence in the literature that antisocial behavior or conduct disorder are associated with adolescent alcohol and drug abuse [Bukstein et al., 1989; Jessor and Jessor, 1975; Jessor and Jessor, 1977; Robins and McEvoy, 1990; Watts and Wright, 1990; Weber et al., 1989; Windle, 1991]. The incidence of antisocial personality is also frequently reported to be higher than population estimates among the relatives of adolescent drug and alcohol abusers. However,

TABLE VII. Estimated Parent–Offspring and Sibling Correlations

	ASB	Depression	Alcohol
Parent–offspring	.263	.173	.191
	.195	.247	.155
	.205	.148	.235
Sibling	.425		
	.203	.462	
	.195	.036	.262

TABLE VIII. Estimated Spousal Correlations

	ASB	Depression	Alcohol
ASB	.57		
Depression	.28	.21	
Alcohol	.38	.17	.31

considerably less is known regarding the association between depression and antisocial behavior, and about the role that depressive symptoms play in adolescent substance abuse. This study investigates the comorbidity of ASB symptoms, depressive symptoms, and alcohol problems in the families of severe substance-abusing adolescents. Our investigations specifically examine the nature of these phenotypic associations by employing multivariate modeling analyses that decompose the phenotypic variation and covariation among these disorders into three primary sources: 1) family factors (genetic and environmental liabilities) that are transmitted from parents to children, 2) residual sibling effects that cannot be explained by vertical familial transmission from parents to children, and 3) nontransmissible factors that are unique to individuals. A particular strength of the family study design used in this investigation is that we also incorporate a matched sample of control families. Most previous family studies of substance abuse have typically used specialized populations without controls. In addition, we directly interviewed all study participants, rather than use less reliable family history approaches that utilize information from a single respondent.

This study confirmed fairly strong within-person phenotypic correlations for ASB symptoms, depressive symptoms, and alcohol problems. In addition, the mean number of problems for each of these disorders was substantially higher among the treatment probands and the first-degree relatives of these substance-abusing adolescents than for a matched control sample of adolescent probands and their first-degree relatives.

Our results suggest that transmissible family factors account for approximately 30–40% of the variance in ASB symptoms, depressive symptoms, and alcohol problems. These findings are consistent with genetic epidemiology studies reporting substantial familial resemblance for these disorders [Grove et al., 1990; Kendler et al., 1993; McGue, 1993; Caspi and Moffitt, 1995]. More important, the transmissible factors underlying these problems are highly intercorrelated. Approximately 50% of the covariation between ASB and alcohol problems, and between ASB and depressive symptoms, could be attributed to transmissible family factors. The correlation between depressive symptoms and alcohol problems (r_t = .58) could be set to zero in our current analyses without significantly affecting model fit (p = .06). However, this was likely due to the relatively low power for testing this correlation with our current sample sizes. These results underscore the importance of investigating potential mechanisms underlying the comorbidity of these disorders.

Interestingly, residual sibling effects, independent of factors transmitted from parents to children (e.g., sibling imitation and/or nonadditive genetic effects) did not contribute to increased sibling resemblance for alcohol problems. Residual sibling effects specific to ASB and depressive symptoms were found. However, our results suggest that these residual sibling effects do not contribute to the covariation among the different psychiatric syndromes. For example, there is no indication in our data that ASB in one sibling influences alcohol abuse in another, or vice versa. The same holds for symptoms of depression and alcohol abuse.

An important caveat to consider, however, is that different measures were used for assessing depressive symptoms and ASB in the adults and juveniles, while alcohol-problem symptoms were assessed using the same instrument. Our findings for alcohol problems are inconsistent with a recent study by McGue et al. [1996], but these researchers also used different measures in adults and adolescents. Without invariant measurement across generations it is impossible to establish conclusive evidence for the presence of sibling effects with our data.

In summary, the results of this study suggest that depressive symptoms may play a role in adolescent ASB and substance abuse. Our analyses firmly indicate that the transmissible familial antecedents underlying ASB and depressive symptoms are significantly intercorrelated. Although the correlation between the family factors underlying depression and alcohol abuse was not statistically significant, the estimate of the correlation was substantial and will need to be tested in larger samples.

Limitations

A number of limitations of the present analyses should be addressed. First, by design the probands were limited to adolescent males, so the reader should be cautioned against generalizing our results to adolescent females. Given the observed sex differences in prevalence rates for the disorders examined in this study, one might obtain different results using female probands and their families. Second, we have assumed that adult antisocial personality symptoms and juvenile conduct disorder symptoms can be used to assess a single dimension of ASB. There is some evidence that juvenile ASB is less heritable than adult antisocial traits [Gottesman and Goldsmith, 1994; Lyons et al., 1995], but this may depend on the onset, severity, and persistence of the behaviors examined [Caspi and Moffitt, 1995; Dishion et al., 1995; Loeber, 1991]. Third, our relatively small sample sizes to date reduce our ability to make strong conclusions from the data. In addition, we were not able to differentiate maternal and paternal transmissible influences in our current analyses, potentially important factors to test as our samples become larger. Finally, although our results suggest that depression shares familial antecedents with ASB and possibly alcohol abuse, depression may be a consequence of substance use and/or involvement with the juvenile justice system (e.g., incarceration), rather than a causal factor. Future analyses may benefit by distinguishing symptoms of primary (i.e., onset preceding symptoms of ASB and substance use) and secondary depression.

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